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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/273,230	03/18/1999	JEFFREY L. CLELAND	P0998D1	6833

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/273,230	CLELAND ET AL.	
	Examiner	Art Unit	
	Christopher H. Yaen	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *20 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,44,46,47 and 51-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,44,46,47 and 51-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Re: Cleland *et al*

1. The amendment filed 10/20/2006 is acknowledged and entered into the record. Accordingly, claims 1-41,43,45, and 48-50 are canceled without prejudice or disclaimer, and claims 53-59 are newly added.

2. Claims 42,44,46-47, and 51-59 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The Information Disclosure Statement filed on 11/22/2006 is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

5. The rejection of claims under 35 USC § 42,44,46-47,51-52, and now newly added claims 53-59 is maintained for the reasons of record. Applicant argues that the instant specification is enabling with regard to a method of using any and all anti-HER2 antibodies. Specifically, applicant argues that the art taught those of skill how to make and use HER2 antibodies that are effective for treating cancer characterized by the over-expression of HER2 receptor. Applicant contends the specification at the time of filing enabled a genus of HER2 antibodies capable of inhibiting tumor cell growth as opposed to the single antibody that stimulates tumor cell growth in Stancovski *et al.* In

addition, applicant contends the Lewis *et al* reference supports the enablement of the instant application because "HRG stimulation of tumor cell growth is inhibited by anti-HER2 Mabs 2C4 and 7F3" thereby increasing the total number of anti-HER2 antibodies that are effective as treatment modalities. Applicant concludes that the enablement of a genus of antibodies is supported by the prior art and by the disclosure of the instant application. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of Mineral Separation v. Hyde, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? A conclusion of lack of enablement means that, based on the evidence regarding each of the *In re Wands* Factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). For example, it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. In this case, however, the specification has exemplified a single antibody at a dosage which has been

described in the specification as being "significantly higher" (see page 2, for example), where the formulation is 2-40 times greater than normal. Such a "higher" dosage has only been exemplified for a single antibody, namely the 4D5 antibody, and therefore the claims are not commensurate in scope to what the specification has provided. It would therefore require undue experimentation to determine the effective dosage for the entire genus of claimed antibodies. Those of skill in the art would cannot extrapolate the teachings of the specification to the enablement of the invention, particularly in the absence of exemplification that is commensurate in scope with the claims, because it is well known that the art of drug discovery and cancer intervention is highly unpredictable. For example, with regard to anticancer drug discovery, Gura (*Science* 1997; 278: 1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile (abstract). Gura teaches that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models, but that only 39 have actually been shown to be useful for chemotherapy (page 1041, first and second paragraphs).

With regard to the cited references, these are general teachings of unpredictability as it pertains to the use of any and all HER2 antibodies. It has been demonstrated that despite the ability of HER2 antibodies to bind and inhibit tumor formation, there are some anti-HER2 antibodies which are capable of promoting tumor cell growth. Because the specification has provided an unusually high dosage of antibody formulation, and the specification has described a single working example, namely 4D5, the specification is not commensurate in scope to the claims. Although it

is clear that the specification need not contain any examples, a single working example does not preclude a rejection stating that enablement is limited to a particular scope. The presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims. In this case, as indicated above, the art of cancer drug discovery is at most unpredictable, and the claims of a method of treating cancer using a "higher" dosage would require empirical discovery and require the skilled artisan to experiment with different HER2 antibodies some of which are incapable of treating and would in fact promote tumor cell growth (see Stancovski *et al).*

Therefore, given the lack of guidance with regard to the broad genus of HER2 antibodies in the treatment of cancer at a higher than normal formulation, one of skill in the art cannot make or use the invention commensurate in scope to the claimed invention. Thus the rejection of claims is maintained.

NEW REJECTION

Claim Rejections - 35 USC § 112, 1st paragraph

6. Claim 54 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

This rejection is essentially the same as that presented in the office action mailed on 5/22/2006 and reiterated here for new claim 54. Applicant has added a new claim reciting a specific dose limitation of "about 80mg/ml to about 400mg/ml" of a HER2 antibody used in a method of treating cancer. The specification as filed does not find support for the specific lower limit of 80 mg/ml. Moreover, the specification as originally filed does not support a range of 80 mg/ml to 400 mg/ml either. The specification on page 22 teaches multiple ranges, including "about 50 mg/ml to about 400mg/ml", "about 80 mg/ml to about 300mg/ml", and "about 90 mg/ml to about 150 mg/ml", however there is not specific range limitation of about 80 mg/ml to about 400 mg/ml nor is there support for 80 mg/ml to about 400 mg/ml as currently claimed. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112.

Applicant has indicated that support for the new limitation is supported by *In re Wertheim*, specifically stating that numerical range limitations from different parts of the specification may be combined. Applicant's arguments have been carefully considered but are not found persuasive. In particular, a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a

subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher Yaen
Art Unit 1643
January 3, 2007

CHRISTOPHER H. YAEN
PRIMARY EXAMINER